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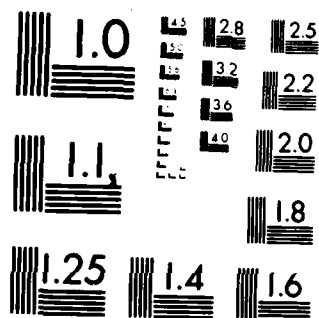   T G WHEELER ET AL. AUG 83 SAM-TR-83-33
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AD-A132 941

DURATION OF MEMORY LOSS DUE TO ELECTRON BEAM EXPOSURE

Thomas G. Wheeler, Ph.D.
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USAF SCHOOL OF AEROSPACE MEDICINE
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NOTICES

This final report was submitted by personnel of the Vulnerability Assessment Branch, Radiation Sciences Division, USAF School of Aerospace Medicine, Aerospace Medical Division, AFSC, Brooks Air Force Base, Texas, under job order 7757-05-E2.
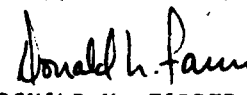
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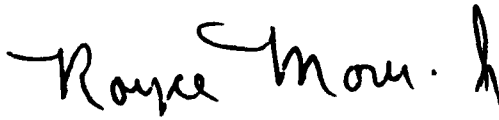
The animals involved in this study were procured, maintained, and used in accordance with the Animal Welfare Act and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources - National Research Council.

The Office of Public Affairs has reviewed this report, and it is releasable to the National Technical Information Service, where it will be available to the general public, including foreign nationals.

This report has been reviewed and is approved for publication.

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20. ABSTRACT *(Continue on reverse side if necessary and identify by block number)*

Electron beam exposure has been shown to produce retrograde amnesia (RA). The objective of this study was to determine the duration of memory loss upon electron beam exposure. It is important to know if exposure produces a memory loss of the events which occurred in the preceding 1 sec or memory loss of the preceding minute's events.

The task was a single-trial avoidance paradigm. The animal was placed in a small aversive chamber. After a 90-sec adaptation period, a door opened that provided

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20. ABSTRACT (Continued)

access to a large, dark, preferred chamber. The time required for the animal to enter the preferred chamber was the measure of interest (T). Once inside the preferred chamber, a 1-sec footshock was delivered. Following the footshock by some preset delay (ΔT), the animal was exposed to a 10-μsec, 10-rad electron beam (or X-ray). A second trial on the task was run 2 hr postexposure. The second trial consisted of placing the animal in the aversive chamber and monitoring the time (T') required to enter the preferred chamber. If the electron beam exposure interfered with the animal's ability to recall the shock, T' would be greatly reduced as compared with the sham controls. The exposure delay times used were ΔT = 1, 3, 5, and 10 sec. RA was produced for ΔT = 1 sec, with decreasing effectiveness for larger ΔT values. For ΔT values greater than 4 sec, electron beam exposure did not produce RA. It was also demonstrated that X-ray exposure (ΔT = 1 sec) produced RA.

Our conclusion was that the RA effect might be due to sensory system activation which provided a novel stimulus that masked previous stimuli (produced RA).

DURATION OF MEMORY LOSS DUE TO ELECTRON BEAM EXPOSURE

INTRODUCTION

The biological effects of particle beams have been studied only in terms of tissue disruption and ionization capabilities at relatively high dose levels. No one would have predicted a biological effect, ionizing or otherwise, at very low doses. However, McNulty and Pease (16) have demonstrated retrograde amnesia (RA) production in mice following an 8-rad exposure. More recently, Wheeler et al. (24) have examined the experimental parameters most effective in amnesia production; they found that RA was produced in a dose range from 0.1 to 10 rad and the most effective dose rate was 10^6 rad/sec.

The objective of the research reported here was to evaluate the duration of retrograde amnesia due to electron beam exposure and to determine if other forms of ionizing radiation also produced RA. It is important to know if exposure to ionizing radiation produces a memory loss of the events which occurred in the preceding 1 sec or memory loss of the preceding minute's events. From an operational standpoint, the difference between a 1-sec and 1-min memory loss could dictate mission completion or failure. The duration of memory loss was evaluated on a behavioral task by varying the time interval between the stimulus to be recalled (footshock) and the pulsed electron beam exposure.

METHODS

The task and apparatus have previously been described in detail (23,24). Briefly, the task was a single-trial avoidance paradigm. The test procedure began when the animal was placed in a small aversive chamber. After a 90-sec adaptation period, a door opened that provided access to a large, dark "preferred" chamber. The time required for the animal to leave the illuminated "aversive" chamber and enter the preferred chamber was the dependent variable (denoted T). Once inside the preferred chamber, a footshock of 85 V (peak to peak) was delivered to the animal for 1 sec. At a preset time delay (ΔT), after the termination of the shock, the linear electron accelerator (LINAC) was pulsed, thus exposing the animal to the electron beam. The animal was then returned to its home cage. A second trial on the same task was run 2 hr postexposure. The second trial consisted of placing the animal in the aversive chamber and monitoring the time (T') required for the animal to enter the preferred chamber. No shock or LINAC pulse was presented on the second trial. If the animal recalled the shock treatment on the first trial, the values of T' (second trial latency) would be large. If the electron beam exposure interfered with the animal's ability to recall the shock, T' would be greatly reduced as compared with the sham controls. The operational definition of RA for this study was the value of T' - T, between the limits of complete recall of the shock (a shock, no exposure condition), and no recall of a shock (no shock presented).

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The data of the control groups provided reference points to which could be compared the data from test groups receiving exposures at various time intervals after the shock (ΔT). The duration between shock and beam exposure (ΔT) was the experimental variable. Radiation exposure consisted of a 10-μsec pulse of either 30-MeV electrons or 30-MeV X-rays. All exposures were 10 ± 1 rad.

A sufficient number of animals (Sprague-Dawley male rats, 175 ± 25 mg) were purchased to make up seven test groups (24 rats/group). The test groups were: electron beam exposure at ΔT = 1, 3, 5, and 10 sec; X-ray exposure at T = 1 sec; and two control groups. The control groups were: (1) No shock but a 10-rad electron beam exposure; to determine if the beam itself was aversive; and (2) Shock and no radiation exposure. The first groups tested were with ΔT = 1 and 5 sec intermixed with sham, shock-only controls. These data dictated the time delays for the next test groups (ΔT = 3 and 10 sec). These groups were also tested intermixed with shock-only controls. The X-ray and no shock groups were tested on the third test day. The animals were maintained on a 12/12 light-dark cycle[1] with free access to food and water.

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[1] It was discovered upon initiation of this study that the rats had been exposed to 10 days of continuous room lighting immediately prior to the test period. Five animals were randomly selected from the population; perfused and retinal sections were prepared and viewed. From these sections, it appears that there was some rod outer segment (ROS) degeneration. The extent of degeneration or how such ROS degeneration would effect flash blindness potential is being evaluated. A complete report on the retinal pathology of these animals is in preparation.

RESULTS

The results are presented in Table 1 and summarized in Figure 1.

TABLE 1. RAW DATA FROM EACH TEST GROUP AND SUMMARY OF DATA. The raw data are T' - T values (in seconds) and the summary of the data include mean, standard deviation (SD), standard error of the mean (SEM), and number of animals per group (N).

Test Condition

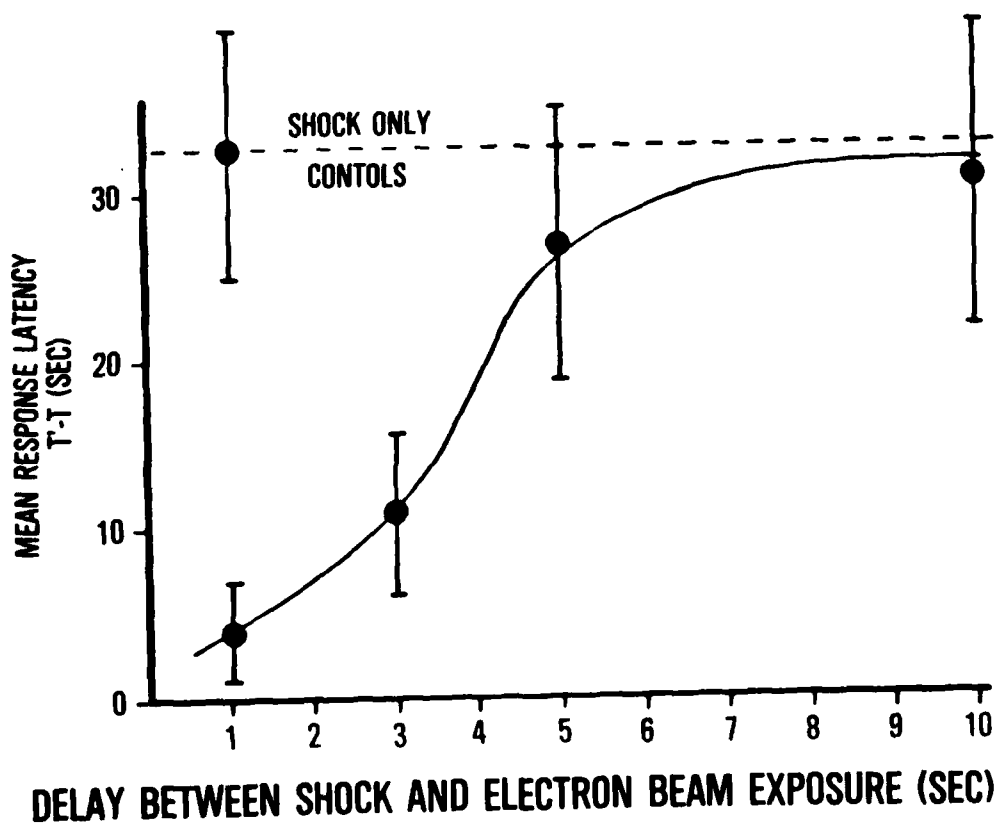|	Shock No Radiation	Electron Beam Exposure $\Delta T =$				X-Ray Exposure $\Delta T = 1$	Electron Exposure No Shock
		1	3	5	10		
	-0.5	-1.5	-0.2	12.5	20.8	14.8	-0.8
	97.0	55.6	40.4	5.5	94.9	-0.3	-3.9
	45.8	0.8	28.7	14.2	-9.7	-8.3	1.8
	30.3	4.4	-2.8	1.9	42.9	6.7	-6.0
	95.0	-2.2	7.7	11.5	9.9	16.6	-1.0
	11.4	-1.0	2.3	95.9	23.9	26.6	-4.0
	9.6	-0.2	9.0	9.9	-3.1	2.0	-1.1
	3.1	-1.6	-0.8	94.9	2.9	-0.2	0.0
	12.5	0.3	18.6	1.5	38.7	0.6	0.2
	23.7	11.6	1.7	2.6	21.2	30.0	-8.7
	15.1	2.0	60.0	11.3	92.0	-0.7	-1.2
	41.4	0.7	-6.5	93.9	6.2		-3.4
	54.7	2.4	-0.4	8.8	37.0		
	9.3	0.2	-0.7	18.1	-1.6		
	3.9	1.3	-3.7	7.9	91.6		
	80.2	-1.4	28.1	92.8			
	13.1	5.9		-0.4			
	44.	4.6		21.8			
		-6.2		21.8			
Mean	32.8	4.0	11.3	26.8	31.2	8.0	-2.4
SD	31.3	13.1	18.9	36.3	35.6	12.3	2.9
SEM	7.4	3.0	4.7	8.3	9.2	2.7	0.8
N	18	19	16	19	15	11	12

Figure 1. Mean response (T' - T) ± SEM.

Experiments such as this which use complicated radiation sources, operating at the limits of their intended design, are prone to malfunctions, thus eliminating subjects from the test groups. For example, on test days 2 and 3 of this study, the linear accelerator malfunctioned a number of times, supplying two rather than one pulse and presenting unwanted pulses before the door opened, etc. In such cases, the experimental animal under test was eliminated from the test group.

DISCUSSION

Numerous findings in the data can be related to previous reports. The most prominent finding is that both electron and X-ray exposure produce RA. This finding provides some indication of possible mechanisms. Since storage of information (memory) is a central nervous system (CNS) function, any stimulus which disrupts memory must activate the CNS. Activation of the CNS occurs normally via the sensory systems, but can also be achieved by experimental manipulations (e.g., local drug injection, temperature changes, induced current, or ionizing radiation). The most likely mechanisms of CNS activation by ionizing radiation exposure are: (a) direct stimulation of CNS neurons via ionization or induced current; or (b) stimulation of one or more of the sensory systems. Each of these possibilities will be considered in turn.

Direct activation of neurons in the CNS via ionization has been shown to require doses greater than 1000 rad across radiation sources, with larger doses producing larger effects (14). The data reported by Wheeler et al. (24) indicate RA production at 0.1 rad, the lowest level tested. This low-dose effect argues against ionization as a mechanism of CNS activation.

Current induction via electroconvulsive shock (ECS) is known to produce RA (15,18). However, no data are available on the amount of current at the neural level required to produce RA. Also unknown is whether the secondary or Compton currents produced by electron beam exposure are qualitatively or quantitatively similar to currents produced by ECS. Although direct comparison between ECS and electron beam currents cannot be made, reports indicate that repeated preexposures to ECS are required to reduce the RA effect (13). In contrast, a single preexposure to an electron beam totally eliminates the RA effect, thus suggesting that CNS activation via induced current was probably not the mechanism of RA production (24). Also, as reported here, X-ray exposure produces RA and X-rays are not known to produce internal currents.

The low-dose effect strongly suggests sensory activation. Every sensory system studied appears to be sensitive to ionizing radiation, some at very low doses (less than 0.1 rad). The olfactory response threshold to ionizing radiation has been shown to be less than 10 mrad (4,5,8). The visual system is sensitive to radiation levels below 0.5 mrad (10,17). Ionizing radiation has been shown to be as efficient as light in producing retinal activity, as monitored by the electroretinogram (1,21,22). Also, sensory systems are primarily sensitive to dose rate, not absolute dose (11). For the visual

system, U-shaped dose-rate response functions are commonly observed (12,19, 20). The olfactory system is more sensitive to dose rate than total dose for low-level X-ray exposures (5). Therefore, an hypothesis is that radiation exposure could have produced RA via activation of one or more of the sensory systems.

Irrespective of how many sensory systems may be involved or the extent of activation of each, exposure would obviously constitute a novel stimulus, particularly since the stimulus was presented in an unfamiliar environment. The "recency theory" appears to apply here. This theory states that, if two or more novel stimuli are sequentially presented, the subject will recall the last stimulus most vividly; i.e., will recall the most recent event (2). In this experiment, two novel stimuli were sequentially presented--a mild shock followed by radiation exposure. When both stimuli were presented, the animal recalled the most recent (forgot the former). When the animal was preexposed to the beam, thereby reducing its novelty, the animal again recalled the most recent novel stimulus, the shock (24).

If radiation exposure produced a novel stimulus via sensory system activation, then activation by conventional stimuli would reasonably be assumed also to produce RA. This theory was tested by a 10^{-6}-sec photoflash in place of electron beam exposure, and RA resulted (23). The same study demonstrated that the extent of RA production was related to photoflash intensity. Also, when the animals were preexposed to a photoflash, the photoflash was no longer an effective amnesiac, just as was the case for electron beam preexposure (24). The duration of memory loss and ability to produce RA with electrons, X-rays, and photoflash supports the contention that the basic mechanism was sensory activation.

Any experiment that utilizes ionizing radiation as a stimulus raises the question of potential biological hazards. Simply stated, we had no indication of harmful effects from the data presented here; i.e., a 10-rad exposure was not aversive, and it has been shown that preexposure eliminated the RA effect (24). This exposure produced no sign of physiological stress and no learning deficit (24). However, other amnesiacs have been shown to be harmful if administered repeatedly (3,6,7,9). The major focus of study here was RA production. The extent to which other biological systems may be affected and the effects of electron beam exposure on other CNS functions remain virtually unknown.

REFERENCES

1. Bachofer, C. S., and S. E. Wittry. Electroretinogram in response to
    X-ray stimulation. Science 133:642-644 (1961).

2. Baddeley, A. D., and G. J. Hitch. Recency reexamined, pp. 647-667. In
    S. Dormic (ed.). Attention and performance VI. New York: John Wiley
    and Sons, 1977.

3. Bartus, R. T. Physostigmine and recent memory: Effects in young and
    aged nonhuman primates. Science 206:1087-1089 (1979).

4. Buchwald, N. A., J. Garcia, B. H. Feder, and G. Bach-y-Rita. Ionizing
    radiation as a perceptual and aversive stimulus, pp. 687-699. In
    T. J. Haley and R. S. Snider (eds.). Response of the nervous system
    to ionizing radiation. Boston, Mass.: Little Brown and Co., 1964.

5. Cooper, G. P. Receptor origin of the olfactory bulb response to ionizing
    radiation. Am J Physiol 215:803-806 (1968).

6. Cronholm, B., and L. Molander. Memory disturbances after electroconvulsive
    therapy: Conditions one month after a series of treatments. Acta
    Psychiatr Scand 40:211-216 (1964).

7. DeWied, D., and B. Bohus. Modulation of memory processes by neuropeptides
    of hypothalmic-neurohypophyseal origin, pp. 139-149. In M. A. B.
    Brazier (ed.). Brain mechanisms in memory and learning. New York:
    Raven Press, 1979.

8. Dinc, H. I., and J. C. Smith. Role of the olfactory bulbs in the detection
    of ionizing radiation by the rat. Physiol Behav 1:139-144 (1966).

9. Flohr, H. Hypoxia-induced retrograde amnesias, pp. 277-291. In M. A. B.
    Brazier (ed.). Brain mechanisms in memory and learning. New York:
    Raven Press, 1979.

10. Gurtovoi, G. K., and Ye. O. Burdianskaia. Visual sensations induced by
    x-irradiation of the eye with doses of the order of one milliroentgen.
    Biophys (USSR) 4:65-71 (1959).

11. Guyton, A. C. Adaptation of receptors. In Basic human physiology (2d ed.).
    Philadelphia: Saunders Co., 1977.

12. Kelly, D. H. Effects of sharp edges in a flickering field. J Opt Soc
    Am 49:730-732 (1959).

13. Kesner, R. P., and J. H. McDonough. Diminished amnestic effect of a
    second electroconvulsive seizure. Exp Neurol 27:527-533 (1970).

14. Kimeldorf, D. J., and E. L. Hunt. Neurophysiological effects of ionizing
    radiation: The central nervous system, pp. 68-69. In Ionizing radia-
    tion: neural function and behavior. New York: Academic Press, 1965.

15. Kopp, R., Z. Bohdanecky, and M. E. Jarvik. Long temporal gradient of retrograde amnesia for a well-discriminated stimulus. Science 153:1547 (1966).

16. McNulty, P., and V. P. Pease. Retrograde amnesia as a function of high dose rate, low-total dose electron beam. Lectures presented at the USAF School of Aerospace Medicine, Weapons Effects Branch, Brooks AFB, Tex., 1981. (Lecturers were faculty members from the Department of Physics, Clarkson College, Potsdam, N.Y.)

17. Pape, R., and J. Zakovsky. Die Roentgen-strahlensensibilitat der Retina. Fortschr Geb Roentgenstr 80:65-71 (1954).

18. Quartermain, D., R. M. Paolino, and N. E. Miller. A brief temporal gradient of retrograde amnesia independent of situational change. Science 149:1116 (1966).

19. Riedemeister, C., and O. J. Grusser. Flimmerlicht-untersuchungen an der Katzenretina. 1. On-Neurone and on-off Neurone. Fur Biol III:241-253 (1959).

20. Schwarz, F. Uber Die Wirkung von Wechselstrom auf des Schorgan. Z. Sinnesphysiol 67:227-244 (1938).

21. Smith J. C., and D. J. Kimeldorf. The bioelectrical response of the insect eye to beta radiation. J Insec Physiol 10:839-847 (1964).

22. Smith, J. C., and H. L. Taylor. Immediate detection of x-rays by the rhesus monkey. Radiat Res 35:528 (1968).

23. Wheeler, T. G. Amnesia production by visual stimulation. USAFSAM-TR-82-45, Dec 1982.

24. Wheeler, T. G., K. A. Hardy, and D. W. Blick. Retrograde amnesia, in rats, produced by electron beam exposure. USAFSAM-TR-83-3, Feb 1983.

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